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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/057,247	01/25/2002	Ethan Lerner	10287-066001 / 1791.1	2777
26161	7590	05/04/2005	EXAMINER KIM, JENNIFER M	
FISH & RICHARDSON PC 225 FRANKLIN ST BOSTON, MA 02110			ART UNIT	PAPER NUMBER

1617  
DATE MAILED: 05/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. 10/057,247	Applicant(s) LERNER ET AL.	
	Examiner Jennifer Kim	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 10 March 2005.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1,2,4,5,7,8,10-11,18,21 and 22 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,4,5,7,8,10-11,18,21 and 22 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>3/10/05</u> . | 6) <input type="checkbox"/> Other: _____  |

*ix*

### **DETAILED ACTION**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/20/2004 has been entered.

### **Action Summary**

The rejection of Claims 1, 3-5, 7 and 9-11 of record rejected under 35 U.S.C. 103 (a) over Lerner et al. (WO 98/33379) in view of Zucchetti et al. (U.S. Patent No. 6,037,481) is hereby expressly withdrawn in view of Applicant's amendment.

The rejection of claims 2 and 8 of record rejected under 35 U.S.C. 103 (a) over Lerner et al. (WO 98/33379) in view of Yamaguchi et al. (EP 0755671A1) is expressly withdrawn in view of Applicant's amendment.

The rejection of claims 18-22 of record rejected under 35 U.S.C. 103 (a) over Lerner et al. (WO 98/33379) in view of Zucchetti et al. (U.S. Patent No. 6,037,481) and further in view of Remington's Pharmaceutical Sciences, 17<sup>th</sup> Edition is expressly withdrawn in view of Applicant's amendment.

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Applicants' amendment necessitates new ground(s) of rejection presented in this Office Action.

***Claim Rejections - 35 USC § 103***

Claims 1, 2, 4, 5, 7, 8, 10, 11, 18, 21 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lerner et al. (WO 98/33379) of record in view of Zucchetti et al. (U.S. Patent No. 6,037,481) of record and further in view of Parab (U.S. Patent No. 5,885,596) and Yamaguchi et al. (EP 0755671A1) of record.

Lerner et al. teach a topical composition comprising Applicants' NOS inhibitor (e.g. L-NAME) for the treatment of unwanted conditions of skin associated with aging in a subject (a human). (abstract, page 2, lines 16-17, page 9, line 34, page 11, lines 26-38, page 13, lines 26-38, page 7, lines 25-29). Lerner et al. teach that L-NAME is useful for the treatment of sunburn or other exposure to ultra-violet light. (page 4, lines 1-5, page 9, lines 33-35, page 11, line 26-page 12, line 4).

Lerner et al. do not expressly teach the treatment of fine wrinkle, the composition as being sterile and ~~the~~ evaluating the effect of the wrinkles, exposure to UVB radiation causing wrinkles and the instructions for the using the composition to prevent wrinkles.

Zucchetti et al. teach that the wrinkles are unwanted effects of the skin aging.

Parab teaches factors such as exposure to the sun or the resulting ultra-violet radiation therefrom contribute to the development of adverse skin conditions such as

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fine wrinkles. (column 1, lines 15-20). Parab teaches fine wrinkles are associated with dermatological ageing. (column 2, lines 46-55).

Yamaguchi et al. disclose that it has been known that the formation of wrinkles is accelerated by exposure to ultraviolet rays, UV-B. (page 2, lines 23-25).

It would have been obvious to one of ordinary skill in the art to modify the Lerner et al.'s method to treat age associated condition such as fine wrinkles with L-NAME because Lerner et al. teach that composition comprising L-NAME is useful for the unwanted conditions of skin associated with aging and that wrinkles including fine wrinkles are the unwanted conditions of the skin aging as taught by Parab and Zucchetti et al. One would have been motivated to make such a modification in order to achieve expected benefit of reducing unwanted aging conditions of skin (e.g. fine wrinkles) as taught by Lerner et al. as modified by Zucchetti et al. and Parab. Absent any evidence to contrary, there would have been a reasonable expectation of successfully treating age related conditions such as fine wrinkles with L-NAME. To provide a sterile composition, and the evaluating the effect of medication to determine prognoses (by evaluating the effect of wrinkles) of the disease condition are all deemed obvious since they are all within the knowledge of the skilled artisan and represent conventional technique to manufacturing formulations to avoid contaminants and the routine performance of the physician to treat patients. Further, it would have been obvious to one of ordinary skill in the art to employ L-NAME for the treatment of fine wrinkles caused by ultra-violet light, UV-B because Lerner teach the treatment of unwanted epidermal or dermal conditions comprising exposure to ultra-violet light and wrinkles are

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the conditions caused by ultra-violet light, UV-B as well-known by Yamaguchi et al.

One would have been motivated to make such a modification to achieve expected benefit of treating a disorder caused by exposure to ultra-violet light (e.g. wrinkles) as generally taught by Lerner et al. Absent any evidence to contrary, there would have been a reasonable expectation of successfully treating wrinkles caused by exposure to ultra-violet light, UV-B with L-NAME to a patient suffering from wrinkles by exposure to ultra-violet light. Moreover, it would have been obvious to one of ordinary skill in the art to include the instruction for using composition to reduce wrinkles and the directions to apply to the skin prior to sun exposure in Learner et al's composition because Learner's composition is effective for unwanted skin condition associated with aging such as fine wrinkles and the conditions (wrinkles) caused by exposure to ultraviolet light as taught by Learner as modified by Zucchetti et al. and Parab. One would have been motivated to include an instruction with Learner's composition to fulfill the responsibility that the patient receive specific instructions precautions, and warnings for safe and effective use of prescribed drugs as the prescriber and the pharmacist.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims are allowed.

***Response to Arguments***

Applicants' arguments filed 1/24/2005 have been fully considered but they are not persuasive. Applicants argue that Lerner teaches that some effects of aging can be treated by decreasing the level of nitric oxide in the skin but it is not inevitable that Lerner teaches that each and every effect of aging or exposure to UV light can be treated in this manner. This is not persuasive because Lerner teaches Applicants' NOS inhibitor (e.g. L-NAME) for the treatment of unwanted conditions of skin associated with aging in a subject (a human) and Lerner et al. also teach that L-NAME is useful for the treatment of sunburn or other exposure to ultra-violet light. This generic teaching to unwanted conditions of skin encompasses fine wrinkles as taught by Zucchetti et al. and Parab, where these references clearly teach that wrinkles including fine wrinkles are associated with unwanted skin aging. Therefore, it would have been obvious to one of ordinary skill in the art to employ L-NAME for the treatment of unwanted skin aging including fine wrinkles with a reasonable expectation of successfully treating conditions related to skin aging (e.g. fine wrinkles). Applicants next argue neither Zucchetti nor Yamaguchi combined with Lerner suggest that wrinkles can be treated by decreasing nitric oxide by increasing proliferation of melanocytes and keratinocytes, or by altering pigmentation. This is not persuasive because Lerner teaches NOS-inhibitors in general including L-NAME are effective for the treatment of skin aging. The utilization of NOS-inhibitors indicates that the effect of inhibiting NOS results in treatment of skin ageing condition. Zucchetti, Parab, and Yamaguchi teach fine wrinkles are the conditions of skin ageing and the conditions can be caused by the exposure to UV-light. Therefore, it

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would have been obvious to one of ordinary skill in the art to employ NOS inhibitor taught by Lerner for the treatment of any skin aging including fine wrinkles since these diseases are conditions of skin ageing. Applicants' cause of fine wrinkles do not patentably distinctive since the treatment of the condition itself (skin aging (e.g. fine wrinkles)) is obvious since Lerner teaches NOS inhibitors are useful for the skin ageing condition. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read 'S. Padmanabhan', with a horizontal line underneath the name.

Sreenivasan Padmanabhan  
Supervisory Examiner  
Art Unit 1617

Jmk  
April 15, 2005